

In re Application of:
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IN THE CLAIMS

Please amend claims 3, 4, 17, and 66, as shown below. Please cancel claims 6-10 without prejudice. The following listing of claims replaces all prior listings.

1-2. (Canceled).

3. (Currently amended) A targeted vesicle composition according to Claim 17 wherein:

X^1 is ~~C(=O)-NH-C(=O)-~~ C(=O)-NH-;

X^2 is ~~C(=O)-~~;

R^1 is acyl having from 16 to 20 carbons;

R^3 is a moiety alkylene having the structure from 1 to 3 carbons $(CH_2)_n$, wherein n is an integer having the value between 1 and 3;

R^4 is acyl having from 16 to 20 carbons; and

R^6 is a direct bond; and

R^7 is ~~lower alkylene~~.

4. (Currently amended) A targeted vesicle composition according to Claim 3 wherein:

R^1 is acyl having from 17 to 19 carbons;

R^3 is methylene; and

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R^4 is acyl having from 17 to 19 carbons; and

R^7 is ethylene.

5-11. (Canceled).

12. (Withdrawn) A targeted vesicle composition according to Claim 11,
wherein:

Xaa is Glycine;

Yaa is Arginine;

Zaa is Serine;

n is 1, 2 or 3; and

m is 1.

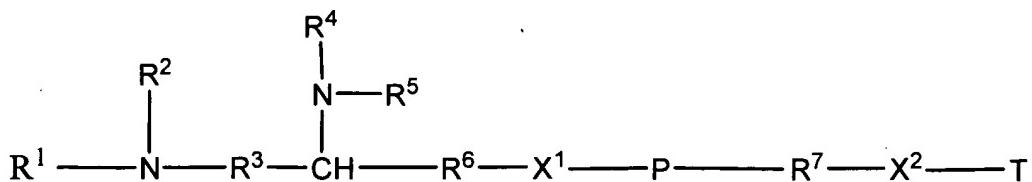
13. (Withdrawn) A targeted vesicle composition according to Claim 12, wherein:

n is 3.

14-16. (Canceled)

17. (Currently amended) A targeted vesicle composition for therapeutic or diagnostic use *in vivo* comprising, in an aqueous carrier, gas filled liposomes comprising a phosphatidylcholine selected from the group consisting of dioleoylphosphatidylcholine, dimyristoylphosphatidylcholine, dipalmitoylphosphatidylcholine and

distearoylphosphatidylcholine, wherein said liposomes further comprise a compound having the formula



(IV)

wherein:

each of X^1 and X^2 is independently a direct bond or a linking atom or group selected from the group consisting of $C(=X^3)$, $C(=X^3)-C(=X^3)$, $C(=X^3)-N(R^8)$, and $C(=X^3)-N(R^8)-C(=X^3)-N(R^8)-C(=X^3)$;

X^2 is $C(=O)$;

X^3 is O or $S-O$ or S ;

R^1 acyl having from 16 to 23 carbons;

R^2 is hydrogen or lower alkyl;

R^3 is a moiety alkylene having the structure from 1 to 10 carbons $(CH_2)_n$, wherein n is an integer having the value between 1 and 10;

R^4 acyl having from 16 to 23 carbons;

R^5 is hydrogen or lower alkyl;

R^6 is a direct bond;

R^7 is $(CH_2)-(CH_2)$ or a direct bond or alkylene having from 1 to 10 carbons;

R^8 is hydrogen or lower alkyl;

P is PEG a hydrophilic polymer; and

T is a targeting ligand comprising a peptide having the sequence CRGDC, wherein the two cysteines are linked together via a disulfide linkage.

18-21. (Canceled).

22. (Previously presented) A targeted vesicle composition according to Claim 17 wherein said phosphatidylcholine comprises dipalmitoylphosphatidylcholine.

23. (Previously presented) A targeted vesicle composition according to Claim 17 further comprising a phosphatidylethanolamine selected from the group consisting of dipalmitoyl-phosphatidylethanolamine, dioleoylphosphatidylethanolamine, N-succinyldioleoyl-phosphatidylethanolamine and 1-hexadecyl-2-palmitoylglycerophosphoethanolamine.

24. (Original) A targeted vesicle composition according to Claim 23 wherein said phosphatidylethanolamine comprises dipalmitoylphosphatidylethanolamine.

25. (Previously presented) A targeted vesicle composition according to Claim 17 further comprising dipalmitoylphosphatidic acid.

26. (Original) A targeted vesicle composition according to Claim 17, wherein said vesicles comprise a gas selected from the group consisting of perfluorocarbons and sulfur hexafluoride.

27. (Original) A targeted vesicle composition according to Claim 26 wherein said perfluorocarbon gas is selected from the group consisting of perfluoromethane, perfluoroethane, perfluoropropane, perfluorobutane and perfluorocyclobutane.

28. (Original) A targeted vesicle composition according to Claim 27 wherein said perfluorocarbon gas is selected from the group consisting of perfluoropropane and perfluorobutane.

29. (Original) A targeted vesicle composition according to Claim 28 wherein said perfluorocarbon gas comprises perfluorobutane.

30. (Original) A targeted vesicle composition according to Claim 17 wherein said gas is derived, at least in part, from a gaseous precursor.

31. (Original) A targeted vesicle composition according to Claim 30 wherein said gaseous precursor has a boiling point of greater than about 37°C.

32. (Original) A targeted vesicle composition according to Claim 31 wherein said gaseous precursor comprises a perfluorocarbon.

33. (Original) A targeted vesicle composition according to Claim 32 wherein said perfluorocarbon is selected from the group consisting of perfluoropentane and perfluorohexane.

34. (Original) A targeted vesicle composition according to Claim 17 wherein said vesicles further comprise a bioactive agent that is different from said gas and said compound.

35. (Original) A targeted vesicle composition according to Claim 34 wherein said bioactive agent comprises a therapeutic agent selected from the group consisting of genetic material, dihydroergotamine, heparin sulfate, tissue plasminogen activator, streptokinase, urokinase, hirudin, and mixtures thereof.

36-60. (Canceled).

61. (Previously presented) A targeted vesicle composition according to Claim 4 wherein:

each of R¹ and R⁴ is acyl of 18 carbons.

62.(Canceled).

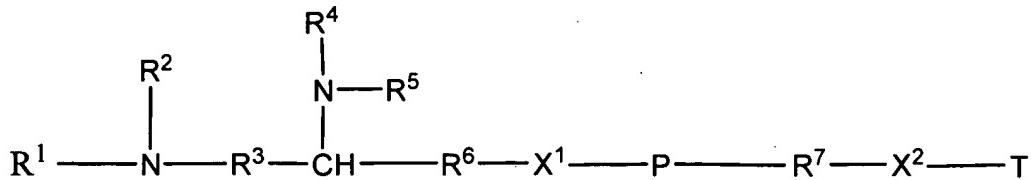
63. (Previously presented) A targeted vesicle composition according to Claim 4 wherein:

R¹ is an acyl of 18 carbons.

64. (Previously presented) A targeted vesicle composition according to Claim 17, wherein said targeting ligand T is a peptide having from 3 to 20 amino acids.

65. (Previously presented) A targeted vesicle composition according to Claim 64, wherein said peptide is cyclized by a linkage selected from the group consisting of sidechain to-sidechain covalent linkages, end-to-sidechain covalent linkages, and end-to-end covalent linkages.

66. (Currently amended) A targeted vesicle composition for therapeutic or diagnostic use *in vivo* comprising, in an aqueous carrier, gas filled liposomes comprising a phosphatidylcholine selected from the group consisting of dioleoylphosphatidylcholine, dimyristoylphosphatidylcholine, dipalmitoylphosphatidylcholine and distearoylphosphatidylcholine, wherein said liposomes further comprise a compound having the formula



wherein:

X^1 is C(=O)-N(R⁸)-C(=X³)-N(R⁸);

X^2 is C(=O) C(=X³);

X^3 is O;

each of R¹ and R⁴ is acyl having 18 carbons;

each of R², R⁵ and R⁸ is H;

each of R³ and R⁷ is ethylene (CH₂)-(CH₂);

R⁶ is a direct bond;

P is PEG-3400; and

T comprises a peptide having the sequence CRGDC, wherein the two cysteines are linked together via a disulfide linkage.

67. (Previously presented) The targeted vesicle composition according to Claim 81, wherein said bioactive agent is urokinase.

68. (Previously presented) The targeted vesicle composition according to Claim 66, wherein said phosphatidylcholine comprises dipalmitoylphosphatidylcholine.

69. (Previously presented) The targeted vesicle composition according to Claim 66, further comprising a phosphatidylethanolamine selected from the group consisting of dipalmitoyl-phosphatidylethanolamine, dioleoylphosphatidylethanolamine, N-succinyldioleoyl-phosphatidylethanolamine and 1-hexadecyl-2-palmitoylglycerophosphoethanolamine.

70. (Previously presented) The targeted vesicle composition according to Claim 69, wherein said phosphatidylethanolamine comprises dipalmitoylphosphatidylethanolamine.

71. (Previously presented) The targeted vesicle composition according to Claim 66, further comprising dipalmitoylphosphatidic acid.

72. (Previously presented) The targeted vesicle composition according to Claim 66, wherein said vesicles comprise a gas selected from the group consisting of perfluorocarbons and sulfur hexafluoride.

73. (Previously presented) The targeted vesicle composition according to Claim 72, wherein said perfluorocarbon gas is selected from the group consisting of perfluoromethane, perfluoroethane, perfluoropropane, perfluorobutane and perfluorocyclobutane.

74. (Previously presented) The targeted vesicle composition according to Claim 73, wherein said perfluorocarbon gas is selected from the group consisting of perfluoropropane and perfluorobutane.

75. (Previously presented) The targeted vesicle composition according to Claim 74, wherein said perfluorocarbon gas comprises perfluorobutane.

76. (Previously presented) The targeted vesicle composition according to Claim 66, wherein said gas is derived, at least in part, from a gaseous precursor.

77. (Previously presented) The targeted vesicle composition according to Claim 76, wherein said gaseous precursor has a boiling point of greater than about 37°C.

78. (Previously presented) The targeted vesicle composition according to Claim 76, wherein said gaseous precursor comprises a perfluorocarbon.

79. (Previously presented) The targeted vesicle composition according to Claim 78, wherein said perfluorocarbon is selected from the group consisting of perfluoropentane and perfluorohexane.

80. (Previously presented) The targeted vesicle composition according to Claim 66, wherein said vesicles further comprise a bioactive agent that is different from said gas and said compound.

81. (Previously presented) The targeted vesicle composition according to Claim 80, wherein said bioactive agent comprises a therapeutic agent selected from the group consisting of genetic material, dihydroergotamine, heparin sulfate, tissue plasminogen activator, streptokinase, urokinase, hirudin, and mixtures thereof.